



# Sequence Listing

<110> Kelley, Robert F.  
Hymowitz, Sarah  
Lindstrom, Stephanie Ho

<120> APO-2 LIGAND/TRAIL VARIANTS AND USES THEREOF

<130> P1966R1

<140> US 10/519,647

<141> 2006-01-10

<150> PCT/US03/019750

<151> 2003-06-23

<150> US 60/391,050

<151> 2002-06-24

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<212> PRT

<213> Homo sapiens

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Val	Ala	Val	Thr	Tyr	Val	Tyr	Phe	Thr	Asn	Glu	Leu	Lys	Gln	Met
				35					40					45

Gln	Asp	Lys	Tyr	Ser	Lys	Ser	Gly	Ile	Ala	Cys	Phe	Leu	Lys	Glu
				50					55					60

Asp	Asp	Ser	Tyr	Trp	Asp	Pro	Asn	Asp	Glu	Glu	Ser	Met	Asn	Ser
				65					70					75

Pro	Cys	Trp	Gln	Val	Lys	Trp	Gln	Leu	Arg	Gln	Leu	Val	Arg	Lys
				80					85					90

Met	Ile	Leu	Arg	Thr	Ser	Glu	Glu	Thr	Ile	Ser	Thr	Val	Gln	Glu
				95					100					105

Lys	Gln	Gln	Asn	Ile	Ser	Pro	Leu	Val	Arg	Glu	Arg	Gly	Pro	Gln
				110					115					120

Arg	Val	Ala	Ala	His	Ile	Thr	Gly	Thr	Arg	Gly	Arg	Ser	Asn	Thr
				125					130					135

Leu	Ser	Ser	Pro	Asn	Ser	Lys	Asn	Glu	Lys	Ala	Leu	Gly	Arg	Lys
				140					145					150

Ile	Asn	Ser	Trp	Glu	Ser	Ser	Arg	Ser	Gly	His	Ser	Phe	Leu	Ser
				155					160					165

Asn	Leu	His	Leu	Arg	Asn	Gly	Glu	Leu	Val	Ile	His	Glu	Lys	Gly
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Phe	Tyr	Tyr	Ile	Tyr	Ser	Gln	Thr	Tyr	Phe	Arg	Phe	Gln	Glu	Glu	
				185					190					195	
Ile	Lys	Glu	Asn	Thr	Lys	Asn	Asp	Lys	Gln	Met	Val	Gln	Tyr	Ile	
				200					205					210	
Tyr	Lys	Tyr	Thr	Ser	Tyr	Pro	Asp	Pro	Ile	Leu	Leu	Met	Lys	Ser	
				215					220					225	
Ala	Arg	Asn	Ser	Cys	Trp	Ser	Lys	Asp	Ala	Glu	Tyr	Gly	Leu	Tyr	
				230					235					240	
Ser	Ile	Tyr	Gln	Gly	Gly	Ile	Phe	Glu	Leu	Lys	Glu	Asn	Asp	Arg	
				245					250					255	
Ile	Phe	Val	Ser	Val	Thr	Asn	Glu	His	Leu	Ile	Asp	Met	Asp	His	
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 aatgggtgaac tgggtcatcca tgaaaaaggg ttttactaca tctattccca 650  
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 aacaaatggt ccaatatatt taaaaatata caagttatcc tgaccctata 750  
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gaagccagtt ttttcggggc ctttttagtt ggctaactga cctggaaaga 950  
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Ala	Ala	Thr	Pro	Ser	Lys	Val	Trp	Gly	Ser	Ser	Ala	Gly	Arg	Ile	35	40	45	
Glu	Pro	Arg	Gly	Gly	Gly	Arg	Gly	Ala	Leu	Pro	Thr	Ser	Met	Gly	50	55	60	
Gln	His	Gly	Pro	Ser	Ala	Arg	Ala	Arg	Ala	Gly	Arg	Ala	Pro	Gly	65	70	75	
Pro	Arg	Pro	Ala	Arg	Glu	Ala	Ser	Pro	Arg	Leu	Arg	Val	His	Lys	80	85	90	
Thr	Phe	Lys	Phe	Val	Val	Val	Gly	Val	Leu	Leu	Gln	Val	Val	Pro	95	100	105	
Ser	Ser	Ala	Ala	Thr	Ile	Lys	Leu	His	Asp	Gln	Ser	Ile	Gly	Thr	110	115	120	
Gln	Gln	Trp	Glu	His	Ser	Pro	Leu	Gly	Glu	Leu	Cys	Pro	Pro	Gly	125	130	135	
Ser	His	Arg	Ser	Glu	Arg	Pro	Gly	Ala	Cys	Asn	Arg	Cys	Thr	Glu	140	145	150	
Gly	Val	Gly	Tyr	Thr	Asn	Ala	Ser	Asn	Asn	Leu	Phe	Ala	Cys	Leu	155	160	165	
Pro	Cys	Thr	Ala	Cys	Lys	Ser	Asp	Glu	Glu	Glu	Arg	Ser	Pro	Cys	170	175	180	
Thr	Thr	Thr	Arg	Asn	Thr	Ala	Cys	Gln	Cys	Lys	Pro	Gly	Thr	Phe	185	190	195	
Arg	Asn	Asp	Asn	Ser	Ala	Glu	Met	Cys	Arg	Lys	Cys	Ser	Thr	Gly	200	205	210	
Cys	Pro	Arg	Gly	Met	Val	Lys	Val	Lys	Asp	Cys	Thr	Pro	Trp	Ser	215	220	225	
Asp	Ile	Glu	Cys	Val	His	Lys	Glu	Ser	Gly	Asn	Gly	His	Asn	Ile	230	235	240	

Trp	Val	Ile	Leu	Val	Val	Thr	Leu	Val	Val	Pro	Leu	Leu	Leu	Val	245	250	255
Ala	Val	Leu	Ile	Val	Cys	Cys	Cys	Ile	Gly	Ser	Gly	Cys	Gly	Gly	260	265	270
Asp	Pro	Lys	Cys	Met	Asp	Arg	Val	Cys	Phe	Trp	Arg	Leu	Gly	Leu	275	280	285
Leu	Arg	Gly	Pro	Gly	Ala	Glu	Asp	Asn	Ala	His	Asn	Glu	Ile	Leu	290	295	300
Ser	Asn	Ala	Asp	Ser	Leu	Ser	Thr	Phe	Val	Ser	Glu	Gln	Gln	Met	305	310	315
Glu	Ser	Gln	Glu	Pro	Ala	Asp	Leu	Thr	Gly	Val	Thr	Val	Gln	Ser	320	325	330
Pro	Gly	Glu	Ala	Gln	Cys	Leu	Leu	Gly	Pro	Ala	Glu	Ala	Glu	Gly	335	340	345
Ser	Gln	Arg	Arg	Arg	Leu	Leu	Val	Pro	Ala	Asn	Gly	Ala	Asp	Pro	350	355	360
Thr	Glu	Thr	Leu	Met	Leu	Phe	Phe	Asp	Lys	Phe	Ala	Asn	Ile	Val	365	370	375
Pro	Phe	Asp	Ser	Trp	Asp	Gln	Leu	Met	Arg	Gln	Leu	Asp	Leu	Thr	380	385	390
Lys	Asn	Glu	Ile	Asp	Val	Val	Arg	Ala	Gly	Thr	Ala	Gly	Pro	Gly	395	400	405
Asp	Ala	Leu	Tyr	Ala	Met	Leu	Met	Lys	Trp	Val	Asn	Lys	Thr	Gly	410	415	420
Arg	Asn	Ala	Ser	Ile	His	Thr	Leu	Leu	Asp	Ala	Leu	Glu	Arg	Met	425	430	435
Glu	Glu	Arg	His	Ala	Lys	Glu	Lys	Ile	Gln	Asp	Leu	Leu	Val	Asp	440	445	450
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Ser Leu Glu

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 ggccgaggag cgctccctac ctccatggga cagcacggac ccagtgcccg 200  
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ctcggtccg ggtccacaag accttcaagt ttgtcgtcgt cggggtcctg 300  
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Gly	Leu	Arg	Val	Pro	Lys	Thr	Leu	Val	Leu	Val	Val	Ala	Ala	Val
				35				40						45

Leu	Leu	Leu	Val	Ser	Ala	Glu	Ser	Ala	Leu	Ile	Thr	Gln	Gln	Asp	50	55	60
Leu	Ala	Pro	Gln	Gln	Arg	Ala	Ala	Pro	Gln	Gln	Lys	Arg	Ser	Ser	65	70	75
Pro	Ser	Glu	Gly	Leu	Cys	Pro	Pro	Gly	His	His	Ile	Ser	Glu	Asp	80	85	90
Gly	Arg	Asp	Cys	Ile	Ser	Cys	Lys	Tyr	Gly	Gln	Asp	Tyr	Ser	Thr	95	100	105
His	Trp	Asn	Asp	Leu	Leu	Phe	Cys	Leu	Arg	Cys	Thr	Arg	Cys	Asp	110	115	120
Ser	Gly	Glu	Val	Glu	Leu	Ser	Pro	Cys	Thr	Thr	Thr	Arg	Asn	Thr	125	130	135
Val	Cys	Gln	Cys	Glu	Glu	Gly	Thr	Phe	Arg	Glu	Glu	Asp	Ser	Pro	140	145	150
Glu	Met	Cys	Arg	Lys	Cys	Arg	Thr	Gly	Cys	Pro	Arg	Gly	Met	Val	155	160	165
Lys	Val	Gly	Asp	Cys	Thr	Pro	Trp	Ser	Asp	Ile	Glu	Cys	Val	His	170	175	180
Lys	Glu	Ser	Gly	Ile	Ile	Ile	Gly	Val	Thr	Val	Ala	Ala	Val	Val	185	190	195
Leu	Ile	Val	Ala	Val	Phe	Val	Cys	Lys	Ser	Leu	Leu	Trp	Lys	Lys	200	205	210
Val	Leu	Pro	Tyr	Leu	Lys	Gly	Ile	Cys	Ser	Gly	Gly	Gly	Gly	Asp	215	220	225
Pro	Glu	Arg	Val	Asp	Arg	Ser	Ser	Gln	Arg	Pro	Gly	Ala	Glu	Asp	230	235	240
Asn	Val	Leu	Asn	Glu	Ile	Val	Ser	Ile	Leu	Gln	Pro	Thr	Gln	Val	245	250	255
Pro	Glu	Gln	Glu	Met	Glu	Val	Gln	Glu	Pro	Ala	Glu	Pro	Thr	Gly	260	265	270
Val	Asn	Met	Leu	Ser	Pro	Gly	Glu	Ser	Glu	His	Leu	Leu	Glu	Pro	275	280	285
Ala	Glu	Ala	Glu	Arg	Ser	Gln	Arg	Arg	Arg	Leu	Leu	Val	Pro	Ala	290	295	300
Asn	Glu	Gly	Asp	Pro	Thr	Glu	Thr	Leu	Arg	Gln	Cys	Phe	Asp	Asp	305	310	315
Phe	Ala	Asp	Leu	Val	Pro	Phe	Asp	Ser	Trp	Glu	Pro	Leu	Met	Arg	320	325	330
Lys	Leu	Gly	Leu	Met	Asp	Asn	Glu	Ile	Lys	Val	Ala	Lys	Ala	Glu	335	340	345
Ala	Ala	Gly	His	Arg	Asp	Thr	Leu	Tyr	Thr	Met	Leu	Ile	Lys	Trp	350	355	360

Val	Asn	Lys	Thr	Gly	Arg	Asp	Ala	Ser	Val	His	Thr	Leu	Leu	Asp
				365					370					375
Ala	Leu	Glu	Thr	Leu	Gly	Glu	Arg	Leu	Ala	Lys	Gln	Lys	Ile	Glu
				380					385					390
Asp	His	Leu	Leu	Ser	Ser	Gly	Lys	Phe	Met	Tyr	Leu	Glu	Gly	Asn
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Ala	Asp	Ser	Ala	Leu	Ser									
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Gly	Pro	Arg	Val	Pro	Lys	Thr	Leu	Val	Leu	Val	Val	Ala	Ala	Val
				35					40					45
Leu	Leu	Leu	Val	Ser	Ala	Glu	Ser	Ala	Leu	Ile	Thr	Gln	Gln	Asp
				50					55					60
Leu	Ala	Pro	Gln	Gln	Arg	Ala	Ala	Pro	Gln	Gln	Lys	Arg	Ser	Ser
				65					70					75
Pro	Ser	Glu	Gly	Leu	Cys	Pro	Pro	Gly	His	His	Ile	Ser	Glu	Asp
				80					85					90
Gly	Arg	Asp	Cys	Ile	Ser	Cys	Lys	Tyr	Gly	Gln	Asp	Tyr	Ser	Thr
				95					100					105
His	Trp	Asn	Asp	Leu	Leu	Phe	Cys	Leu	Arg	Cys	Thr	Arg	Cys	Asp
				110					115					120
Ser	Gly	Glu	Val	Glu	Leu	Ser	Pro	Cys	Thr	Thr	Thr	Arg	Asn	Thr
				125					130					135
Val	Cys	Gln	Cys	Glu	Glu	Gly	Thr	Phe	Arg	Glu	Glu	Asp	Ser	Pro
				140					145					150
Glu	Met	Cys	Arg	Lys	Cys	Arg	Thr	Gly	Cys	Pro	Arg	Gly	Met	Val
				155					160					165
Lys	Val	Gly	Asp	Cys	Thr	Pro	Trp	Ser	Asp	Ile	Glu	Cys	Val	His
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Lys	Glu	Ser	Gly	Thr	Lys	His	Ser	Gly	Glu	Ala	Pro	Ala	Val	Glu
				185					190					195
Glu	Thr	Val	Thr	Ser	Ser	Pro	Gly	Thr	Pro	Ala	Ser	Pro	Cys	Ser
				200					205					210
Leu	Ser	Gly	Ile	Ile	Ile	Gly	Val	Thr	Val	Ala	Ala	Val	Val	Leu
				215					220					225

Ile	Val	Ala	Val	Phe	Val	Cys	Lys	Ser	Leu	Leu	Trp	Lys	Lys	Val	230	235	240
Leu	Pro	Tyr	Leu	Lys	Gly	Ile	Cys	Ser	Gly	Gly	Gly	Gly	Asp	Pro	245	250	255
Glu	Arg	Val	Asp	Arg	Ser	Ser	Gln	Arg	Pro	Gly	Ala	Glu	Asp	Asn	260	265	270
Val	Leu	Asn	Glu	Ile	Val	Ser	Ile	Leu	Gln	Pro	Thr	Gln	Val	Pro	275	280	285
Glu	Gln	Glu	Met	Glu	Val	Gln	Glu	Pro	Ala	Glu	Pro	Thr	Gly	Val	290	295	300
Asn	Met	Leu	Ser	Pro	Gly	Glu	Ser	Glu	His	Leu	Leu	Glu	Pro	Ala	305	310	315
Glu	Ala	Glu	Arg	Ser	Gln	Arg	Arg	Arg	Leu	Leu	Val	Pro	Ala	Asn	320	325	330
Glu	Gly	Asp	Pro	Thr	Glu	Thr	Leu	Arg	Gln	Cys	Phe	Asp	Asp	Phe	335	340	345
Ala	Asp	Leu	Val	Pro	Phe	Asp	Ser	Trp	Glu	Pro	Leu	Met	Arg	Lys	350	355	360
Leu	Gly	Leu	Met	Asp	Asn	Glu	Ile	Lys	Val	Ala	Lys	Ala	Glu	Ala	365	370	375
Ala	Gly	His	Arg	Asp	Thr	Leu	Tyr	Thr	Met	Leu	Ile	Lys	Trp	Val	380	385	390
Asn	Lys	Thr	Gly	Arg	Asp	Ala	Ser	Val	His	Thr	Leu	Leu	Asp	Ala	395	400	405
Leu	Glu	Thr	Leu	Gly	Glu	Arg	Leu	Ala	Lys	Gln	Lys	Ile	Glu	Asp	410	415	420
His	Leu	Leu	Ser	Ser	Gly	Lys	Phe	Met	Tyr	Leu	Glu	Gly	Asn	Ala	425	430	435
Asp	Ser	Ala	Met	Ser											440		

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<212> PRT

<213> Homo sapiens

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Ile	Asn	Ser	Trp	Glu	Ser	Ser	Arg	Ser	Gly	His	Ser	Phe	Leu	Ser	35	40	45	
Asn	Leu	His	Leu	Arg	Asn	Gly	Glu	Leu	Val	Ile	His	Glu	Lys	Gly	50	55	60	



Phe	Tyr	Tyr	Ile	Tyr	Ser	Gln	Thr	Tyr	Phe	Arg	Phe	Gln	Glu	Glu	
				65					70					75	
Ile	Lys	Glu	Asn	Thr	Lys	Asn	Asp	Lys	Gln	Met	Val	Gln	Tyr	Ile	
				80					85					90	
Tyr	Lys	Tyr	Thr	Ser	Tyr	Pro	Asp	Pro	Ile	Leu	Leu	Met	Lys	Ser	
				95					100					105	
Ala	Arg	Asn	Ser	Cys	Trp	Ser	Lys	Asp	Ala	Glu	Tyr	Gly	Leu	Tyr	
				110					115					120	
Ser	Ile	Tyr	Gln	Gly	Gly	Ile	Phe	Glu	Leu	Lys	Glu	Asn	Asp	Arg	
				125					130					135	
Ile	Phe	Val	Ser	Val	Thr	Asn	Glu	His	Leu	Ile	Asp	Met	Asp	His	
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Phe	Ser	Leu	Ser	Asn	Asn	Ser	Leu	Leu	Val	Pro	Thr	Ser	Gly	Ile	
				35					40					45	
Tyr	Phe	Val	Tyr	Ser	Gln	Val	Val	Phe	Ser	Gly	Lys	Ala	Tyr	Ser	
				50					55					60	
Pro	Lys	Ala	Thr	Ser	Ser	Pro	Leu	Tyr	Leu	Ala	His	Glu	Val	Gln	
				65					70					75	
Leu	Phe	Ser	Ser	Gln	Tyr	Pro	Phe	His	Val	Pro	Leu	Leu	Ser	Ser	
				80					85					90	
Gln	Lys	Met	Val	Tyr	Pro	Gly	Leu	Gln	Glu	Pro	Trp	Leu	His	Ser	
				95					100					105	
Met	Tyr	His	Gly	Ala	Ala	Phe	Gln	Leu	Thr	Gln	Gly	Asp	Gln	Leu	
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Ser	Thr	His	Thr	Asp	Gly	Ile	Pro	His	Leu	Val	Leu	Ser	Pro	Ser	
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Thr	Val	Phe	Phe	Gly	Ala	Phe	Ala	Leu							
				140											

<210> 9  
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<400> 9

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Leu	Gln	Trp	Leu	Asn	Arg	Arg	Ala	Asn	Ala	Leu	Leu	Ala	Asn	Gly	20	25	30	
Val	Glu	Leu	Arg	Asp	Asn	Gln	Leu	Val	Val	Pro	Ser	Glu	Gly	Leu	35	40	45	
Tyr	Leu	Ile	Tyr	Ser	Gln	Val	Leu	Phe	Lys	Gly	Gln	Gly	Cys	Pro	50	55	60	
Ser	Thr	His	Val	Leu	Leu	Thr	His	Thr	Ile	Ser	Arg	Ile	Ala	Val	65	70	75	
Ser	Tyr	Gln	Thr	Lys	Val	Asn	Leu	Leu	Ser	Ala	Ile	Lys	Ser	Pro	80	85	90	
Cys	Gln	Arg	Glu	Thr	Pro	Glu	Gly	Ala	Glu	Ala	Lys	Pro	Trp	Tyr	95	100	105	
Glu	Pro	Ile	Tyr	Leu	Gly	Gly	Val	Phe	Gln	Leu	Glu	Lys	Gly	Asp	110	115	120	
Arg	Leu	Ser	Ala	Glu	Ile	Asn	Arg	Pro	Asp	Tyr	Leu	Leu	Phe	Ala	125	130	135	
Glu	Ser	Gly	Gln	Val	Tyr	Phe	Gly	Ile	Ile	Ala	Leu	140	145					

<210> 10  
 <211> 141  
 <212> PRT  
 <213> Homo sapiens

Gln	Ile	Ala	Ala	His	Val	Ile	Ser	Glu	Ala	Ser	Ser	Lys	Thr	Thr	1	5	10	15
Ser	Val	Leu	Gln	Trp	Ala	Glu	Lys	Gly	Tyr	Tyr	Thr	Met	Ser	Asn	20	25	30	
Asn	Leu	Val	Thr	Leu	Glu	Asn	Gly	Lys	Gln	Leu	Thr	Val	Lys	Arg	35	40	45	
Gln	Gly	Leu	Tyr	Tyr	Ile	Tyr	Ala	Gln	Val	Thr	Phe	Cys	Ser	Asn	50	55	60	
Arg	Glu	Ala	Ser	Ser	Gln	Ala	Pro	Phe	Ile	Ala	Ser	Leu	Cys	Leu	65	70	75	
Lys	Ser	Pro	Gly	Arg	Phe	Glu	Arg	Ile	Leu	Leu	Arg	Ala	Ala	Asn	80	85	90	
Thr	His	Ser	Ser	Ala	Lys	Pro	Cys	Gly	Gln	Gln	Ser	Ile	His	Leu	95	100	105	
Gly	Gly	Val	Phe	Glu	Leu	Gln	Pro	Gly	Ala	Ser	Val	Phe	Val	Asn	110	115	120	
Val	Thr	Asp	Pro	Ser	Gln	Val	Ser	His	Gly	Thr	Gly	Phe	Thr	Ser	125	130	135	

Phe Gly Leu Leu Lys Leu  
140

<210> 11  
<211> 137  
<212> PRT  
<213> Homo sapiens

<400> 11  
Arg Lys Val Ala His Leu Thr Gly Lys Ser Asn Ser Arg Ser Met  
1 5 10 15  
Pro Leu Glu Trp Glu Asp Thr Tyr Gly Ile Val Leu Leu Ser Gly  
20 25 30  
Val Lys Tyr Lys Lys Gly Gly Leu Val Ile Asn Glu Thr Gly Leu  
35 40 45  
Tyr Phe Val Tyr Ser Lys Val Tyr Phe Arg Gly Gln Ser Cys Asn  
50 55 60  
Asn Leu Pro Leu Ser His Lys Val Tyr Met Arg Asn Ser Lys Tyr  
65 70 75  
Pro Gln Asp Leu Val Met Met Glu Gly Lys Met Met Ser Tyr Cys  
80 85 90  
Thr Thr Gly Gln Met Trp Ala Arg Ser Ser Tyr Leu Gly Ala Val  
95 100 105  
Phe Asn Leu Thr Ser Ala Asp His Leu Tyr Val Asn Val Ser Glu  
110 115 120  
Leu Ser Leu Val Asn Phe Glu Glu Ser Gln Thr Phe Phe Gly Leu  
125 130 135

Tyr Lys

<210> 12  
<211> 152  
<212> PRT  
<213> Homo sapiens

<400> 12  
Gln Pro Phe Ala His Leu Thr Ile Asn Ala Thr Asp Ile Pro Ser  
1 5 10 15  
Gly Ser His Lys Val Ser Leu Ser Ser Trp Tyr His Asp Arg Gly  
20 25 30  
Trp Ala Lys Ile Ser Asn Met Thr Phe Ser Asn Gly Lys Leu Ile  
35 40 45  
Val Asn Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe  
50 55 60  
Arg His His Glu Thr Ser Gly Asp Leu Ala Thr Glu Tyr Leu Gln  
65 70 75  
Leu Met Val Tyr Val Thr Lys Thr Ser Ile Lys Ile Pro Ser Ser  
80 85 90

His	Thr	Leu	Met	Lys	Gly	Gly	Ser	Thr	Lys	Tyr	Trp	Ser	Gly	Asn
				95					100					105
Ser	Glu	Phe	His	Phe	Tyr	Ser	Ile	Asn	Val	Gly	Gly	Phe	Phe	Lys
				110					115					120
Leu	Arg	Ser	Gly	Glu	Glu	Ile	Ser	Ile	Glu	Val	Ser	Asn	Pro	Ser
				125					130					135
Leu	Leu	Asp	Pro	Asp	Gln	Asp	Ala	Thr	Tyr	Phe	Gly	Ala	Phe	Lys
				140					145					150

Val Arg

<210> 13

<211> 36

<212> DNA

<213> Artificial sequence

<220>

<223> sequence is synthesized

<400> 13

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